REMARKS

The Amendments

Claims 14 and 19 are amended to address the rejection under 35 U.S.C. §112, second paragraph. Support for the recitation of mixing of the components is found in the specification, for example, in the preparation examples at pages 39-42. Claim 15 is canceled.

Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Rejections under 35 U.S.C. §112, second paragraph

The rejections of claims 14 and 17 and of claim 15 under 35 U.S.C. §112, second paragraph, are believed to be rendered moot by the above amendments. It is clear that the first rejection was intended to be of claims 14 and 19 and those claims have been amended in the manner suggested in the Office action to remove the term giving rise to the objection. Claim 15 is canceled rendering the rejection thereof moot.

The Rejection under 35 U.S.C. §112, first paragraph

The rejection of claim 15 under 35 U.S.C. §112, first paragraph, for lack of enablement of methods for treating type 1 diabetes, is respectfully traversed. Claim 15 is canceled but it is evident that the rejection was intended to be directed to claim 16 as well. Thus, the rejection as applied to claim 16 is traversed as follows.

Applicants urge that the specification together with the knowledge available to one of ordinary skill in the art supports adequate enablement of the method for treating type 1 diabetes according to the invention. Applicants refer to the Pospisilik reference (*Diabetes*, Vol. 52, March 2003, pp.741-750) which was made of record in the IDS filed March 7, 2008. In Pospisilik, the authors provide evidence showing a connection between DPP IV inhibitor effect and treatment of type 1 diabetes. The connection of DPP IV inhibitor effect to treatment of type 2 diabetes was already established and this article is an example of the acceptance in the art of a connection between DPP IV inhibitor effect and treating type 1 diabetes as well. The specification provides data showing that compounds according to the claimed invention and representative of the claimed scope exhibit DPP IV inhibiting activity; see, e.g., pages 23-24, of the specification. The specification also states the connection between such DPP IV inhibiting activity and treating type 1 diabetes, e.g., at page 24. This statement is further supported by the Pospisilik reference and there is no evidence of record which refutes such a connection.

In order to support a rejection under 35 U.S.C. §112, first paragraph, for lack of enablement, the burden lies first with the PTO to provide evidence or objective reasoning substantiating the allegation that the enabling disclosure is not commensurate in scope with the claims. See, e.g., MPEP §2164.04 citing In re Marzocchi et al., 169 USPQ 367 (CCPA 1971), which states:

> ".. a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented ***must*** be taken as in compliance with the enabling requirement of the first paragraph of §112 ***unless*** there is reason to doubt the objective truth of the statements contained therein..",

and further,

> "..it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." (emphasis original).

Although applicants note the discussion of the Wands factors in the Office action – and address these below – applicants also note that the PTO has not provided any actual evidence which refutes or raises doubts about the truth or accuracy of the inventors' statements in the specification that the compounds are useful for treating type 1 diabetes. There is also no explanation of *why* the PTO doubts the truth or accuracy of the inventors' statements. Thus, applicants urge that – despite the Wands factors – the PTO has not met its initial burden of proof to support a lack of enablement rejection.

In view of the above, applicants submit that the enablement rejection is adequately traversed. But the following comments on the Wands factors discussed in the Office action are provided to further support applicants' position. The scope of the claims is not unreasonably broad, as apparently recognized by the statement in the Office action that the claims are directed to a limited number of species. Further, the scope of the methods is limited to treating only three specific conditions. Thus, the scope is quite specifically defined as to the particular uses as well. These factors support enablement. As for predictability and the nature of the invention, applicants urge that the mere fact that the invention relates to the medical field does not support unpredictability in the current state of the art. The cited Fisher case was nearly 40 years ago and it is no longer the case that all inventions in the medical field are considered unpredictable to the

extend of supporting lack of enablement. Regarding direction and guidance from the specification, this is discussed above, i.e., the showing of DPP IV inhibition and its connection to treating specific conditions. Further, the claims are limited to treating three specific conditions which are well characterized in the art. Thus, dosing of the compounds within the dose range provided would be routine to one of ordinary skill in the art. The Office action alleges for state of the prior art that there is no teaching of similar compounds for treating such conditions. However, there is evidence to support that DPP IV inhibitors have a nexus to treating the claimed conditions, including diabetes type 1, and applicants have shown that the compounds have DPP IV inhibiting activity. Further, the connection already known in the art between DPP IV inhibition and type 1 diabetes treatment is counter to a high level of unpredictability. Regarding working examples, it is not required that applicants provide working examples of the actual method. The showing of DPP IV inhibition effect is sufficient guidance to provide a reasonable expectation of success in view of the connection between DPP IV inhibition and type 1 diabetes treatment. The level of one of ordinary skill in the art for this art would be at a high level and, thus, supports a finding of enablement. One skilled in this art, e.g., an endocrinologist, would be highly educated, i.e., Ph.D. level, and very familiar with the treatment and pathology of type 1 diabetes. The difficultly of achieving success alleged in the Office action and the severity and frequency of the conditions requiring treatment dictate that those trying to solve these problems would be at a very high level, not low level. Further, such ordinary skilled artisan would understand that symptoms of diabetes type 1 will manifest sometime before a patient's insulin-producing pancreatic islets are totally destroyed and the patient will continue to produce insulin until the disease destroys all the patient's pancreatic islets. At least in this period between

diagnosis of diabetes type and absolute insulin deficiency, a DPP IV inhibitor can be used to treat diabetes type 1 by promoting an increased serum insulin level. In view of all of these factors, it is urged that the quantity of experimentation needed for one of ordinary skill in the art to make and use the claimed invention would not be undue. That some experimentation may be necessary does not support a lack of enablement, as long as the experimentation needed is routine or not undue. That is the case here.

For the above reasons, it is urged that the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,
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Attorney Docket No.: 1/1386

Date: May 12, 2008
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